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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/026,992	12/19/2001	David Bebbington	VPI/00-130-4	2621

7590 01/19/2007

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EXAMINER	
RAO, DEEPAK R	
ART UNIT	PAPER NUMBER
1624	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/026,992	BEBBINGTON ET AL.	
	Examiner	Art Unit	
	Deepak Rao	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,14,16,17,20,22 and 27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,14,16,17,20,22 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 1, 2006 has been entered.

Claims 1-11, 14, 16-17, 20, 22 and 27 are pending in this application.

Withdrawn Rejections/Objections:

Applicant is notified that any outstanding rejection/objection that is not expressly maintained in this office action has been withdrawn or rendered moot in view of applicant's amendments and/or remarks.

The following rejections are maintained:

1. Claim 11 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of colon cancer, does not reasonably provide enablement for the treatment of all other diseases embraced by the instant claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The reasons provided in the previous office action are incorporated here by reference.

Applicant's arguments have been fully considered but they were not deemed to be

persuasive. Applicant argues that 'claim 11 is enabled for inhibiting Aurora-2, GSK-3 or Src activity in the recited biological samples'. The claim continues to be open ended to include many and all types of biological samples, as the language includes, for example, "cell cultures and extracts thereof; biopsied material obtained from mammals or extracts thereof". The claim continues to be in a 'reach through' format as being drawn to mechanistic, receptor binding or enzymatic functionality, for which they lack written description and enabling disclosure in the specification thereby requiring undue experimentation for one of skill in the art to practice the invention.

As can be seen from the definition of the term "biological sample" and the purpose of the inhibition of Aurora-2, GSK-3 or Src activity which includes for example, blood transfusion, organ-transplantation, etc. As the inhibition of Aurora-2, GSK-3 or Src activity in a biological sample is disclosed to be useful for blood transfusion, organ-transplantation, etc., it implicitly reads on the inherent therapeutic methods characterized by the activity, which as per the specification includes numerous types of disorders. The use disclosed for the compounds of the invention is as therapeutic agents and the specification does not provide any other purpose or utility based on the activity of the compounds. Therefore, it is maintained that the instant claim continues to be directed towards the treatment of diverse diseases disclosed in the specification.

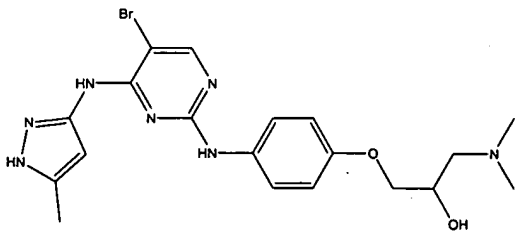
Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the use of the invention. In view of the breadth of the claim, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have

to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

2. Claims 1-11, 14, 16-17, 20, 22 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bradbury et al., WO 00/39101 **or** Armistead et al., WO 01/60816 **or** Pease et al., WO 01/64655. The reasons provided in the previous office action are incorporated hereby reference.

Applicant did not set forth any arguments in the response filed on December 1, 2006. Applicant's arguments in previous response filed on February 28, 2006 were fully addressed in the previous office action, and continue to be applicable to the claims. The reasons from the previous office action are provided below for convenience.

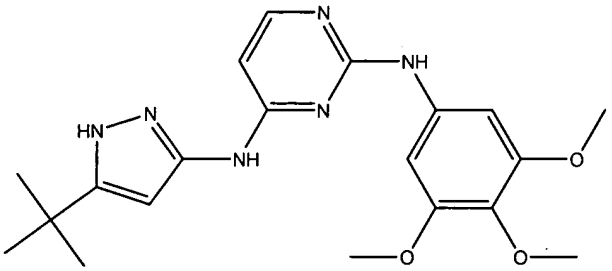
> Applicant's arguments have been fully considered but they were not deemed to be persuasive. Applicant cites MPEP § 2143 and argues that 'to establish a prima facie case of obviousness, there must be some suggestion or motivation; reasonable expectation of success; and the prior must teach or suggest all the claim limitation'. As indicated in the previous office action, all of the above conditions required to establish a prima facie case of obviousness have been met. The references individually teach pyrazolyl substituted pyrimidine compounds, which are disclosed, to have kinase inhibitory activity. See, for example, WO 00/39101 formula I in page 2 and the species of Example 135 (depicted below for convenience):



1-[4-[[5-bromo-4-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]amino]phenoxy]-3-(dimethylamino)-2-propanol

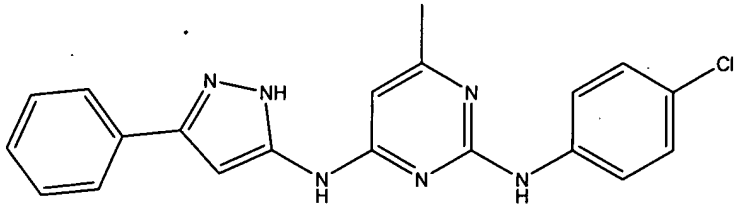
The instant claim on the other hand recite that the substituent at the 6-position (R^y) can be a halo, e.g., bromo, while the substituent at the 5-position (R^x) can be hydrogen. Therefore, the instantly claimed compounds differ from the reference compounds by the position of the substituent and are therefore, positional isomers.

Similarly, WO 01/60816 discloses a compound (depicted below for convenience):



N4-[5-(1,1dimethylethyl)-1H-pyrazol-3-yl]-N2-(3,4,5-trimethoxyphenyl)-2,4-pyrimidinediamine

The instant claims differ from the above compound by having a substituent (R^y) which can be a C_{1-6} aliphatic group, e.g., a methyl group. See, for example, claim 8, the eleventh compound (page 9, lines 11-12) (depicted below for convenience):



[2-(4-chlorophenyl)amino-6-methyl-pyrimidin-4-yl]-(5-phenyl-2H-pyrazol-3-yl)-amine

Therefore, the instantly claimed compounds differ from the reference compounds by a $-CH_2$ group and are therefore, structural homologs of the reference compounds.

In other words, the instant claims differ from the reference compounds as being structural isomers or homologs. It has been held that compounds that are structurally analogous to prior art compounds are *prima facie* obvious, absent a showing of unexpected results.

The reference compounds are taught to be useful as pharmaceutical agents having kinase inhibitory activity, which is the same use recited for the instant

claims. "When chemical compounds have 'very close' structural similarities, without more a *prima facie* case may be made", see *In re Wilder*, 563 F.2d 457, 195 USPQ 426 (CCPA 1977) (adjacent homologs and structural isomers). "When such 'close' structural similarity to prior art compounds is shown, in accordance with these precedents the burden of coming forwards shifts to the applicant, and evidence affirmatively supporting unobviousness is required", *In re Grabiak*, 769 F.2d 729, 731, 226 USPQ 870, 871 (Fed. Cir. 1985). Thus, case law supports the position that a claimed chemical compound suggests a positional isomer thereof (i.e., structurally analogous compounds differing from the reference compounds by the position of substituent); or a structural homolog thereof (i.e., a structurally analogous compounds differing from the reference compound by a $-CH_2$ group) and therefore renders those positional isomers or structural homologs *prima facie* obvious.

"An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a claimed compound, in the expectation that compounds similar in structure will have similar properties." *In re Payne*, 606 F.2d 303, 313, 203 USPQ 245, 254 (CCPA 1979). Reference must be considered under 35 U.S.C. 103, not only for what it expressly teaches but also for what it fairly suggests, in determining obviousness. *In re Burckel*, 201 USPQ 67 (CCPA 1979). If the prior art compound does in fact possess a particular benefit, even though the benefit is not recognized in the prior art, applicant's recognition of the benefit is not in itself sufficient to distinguish the claimed compounds from the prior art. The reference teaches a use for the compounds, which is sufficient to one of ordinary skill to make the claimed compounds because similar properties are normally presumed when compounds are very close in structure.

Contrary to applicant's arguments based on MPEP 2143.01, each of the references, **individually** taught and disclosed compounds that are structurally analogous to the instantly claimed compounds, see the structures depicted above. "Structural relationships provide the requisite motivation or suggestion to modify

known compounds to obtain new compounds." See *In re Duel*, 51 F.3d at 1558, 34 USPQ2d at 1214. The closer the physical and chemical similarities between the claimed species or subgenus and any exemplary species or subgenus disclosed in the prior art, the greater the expectation that the claimed subject matter will function in an equivalent manner to the genus. See *In re Dillon*, 919 F.2d at 696, 16 USPQ2d at 1904.

It is maintained that one of ordinary skill in the art would have been motivated to pre pare the instantly claimed compounds that differ from the reference compounds by having a hydrogen in place of the methyl, with the reasonable expectation that such structurally analogous compounds would have similar properties and therefore, the same use as taught for the reference compounds, in the absence of a showing to the contrary.

Conclusion

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Monday-Friday from 8:00am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Deepak Rao
Primary Examiner
Art Unit 1624

January 11, 2007